

Herbal Medicine as Paradigm for Hepatoprotection: A Comprehensive Review

Asha Singh and Rajesh Singh Tomar

Amity Institute of Biotechnology, Amity University Madhya Pradesh, Gwalior India

Mail I'd asingh@gwa.amity.edu

ABSTRACT

India is sitting on a gold mine of well-recorded and well-practiced knowledge of traditional herbal medicine. Herbal medicine these days has become more popular partly because of scientific validation of some of their medicinal values. It is still an important pillar of about 75–90% globally, primarily in the developing countries, for essential medical care as a result of well social acceptability, superior compatibility with the human body. There are thousands of plant species having good potential of offering direct therapeutic effect individually or in combinations. Herbal medicines are considered as state-of-art laboratories proficient of biogenic synthesis of nanoparticles through different chemical classes. Many of these are proved to be precursors for development of other drugs. Furthermore, many western drugs have their origin through herbal extracts. Numerous herbal agents, effectively used for gastrointestinal, cardiovascular, nervous and metabolic disorders. A vast majority of plants has been examined for hepatoprotective potential, many of them with well-known proven capacity to combat hepatic dysfunction. Therefore, an attempt to harness the potency of plants to develop new hepatoprotective drugs has become the need of the era.

Keywords: Herbal Medicine; Bioactive compounds; Hepatoprotection

Introduction

Plants assume a crucial part in sustaining health of anthropoid and contribute towards progress of human existence. They are significant segments of medications, beauty care products, colors, refreshments, dyes and so forth. As of late, center around herbal research has been expanded everywhere on the globe immensely. There are thousands of plant species having good potential of offering direct therapeutic effect individually or in combinations. Plants are considered as state-of-art chemical laboratories fit for biosynthesizing number of biomolecules of various synthetic classes. Many of these are proved to be precursors for development of other drugs [1]. Furthermore, many western drugs have their origin through plant extracts. Numerous herbal drugs, which are effectively castoff for gastrointestinal, cardiovascular, nervous and metabolic disorders. Ethno-botanical and ethno-pharmacological studies on such plants continue to attract investigators throughout the world [2].

Medicinal plants belonging to about 44 families are investigated for hepatoprotection and morethan 1.5 million specialists are using the traditional remedial method for health care [3,4]. It is estimated that about 7800 industrialized entities are involved in the manufacture of herbal products [5-6]. A single drug can not be operative for the sever liver diseases [7]. In this manner, a compelling

definition must be created utilizing native therapeutic plants, with appropriate pharmacological analyses and clinical preliminaries [8]. Polyherbal therapy is said to be a pharmacological principle having the advantage of producing maximum therapeutic compounds with minimum side effects (Aslam). Despite the tremendous strides in modern medicine, there are rare medications that stimulate liver function, offer protection to the liver from damage or help to regenerate hepatic cells. The WHO is engaged to establish definitive guidelines for methodology of clinical research and the appraisal of effectiveness of traditional medicines [9,10]. Therefore in the present review investigate the ameliorative effect of herbal drugs to mitigate hepatotoxicity.

Herbal Medicine and Health

Wellbeing is a state of complete mental, physical and communal opulence and not just the shortfall of illness. Characteristic plant items have been utilized empirically for protective action since ancient times and tendency is emerging today for their increased use. Contribution of the traditional medicine to human health in the 21st Century is of paramount importance. Herbal drugs create a chief share of all the legitimately recognized systems of health in India viz. *Ayurveda, Yoga, Unani, Siddha*, Homeopathy and Naturopathy except Allopathy. Majority of India's population still use these non-allopathic medical systems. In India about 2,500 plants species are known to be useful and more than 6,000 manufacturers produce about 1,500 medicinal preparations from plants [11].

World population in the current growth rate is likely to reach 11.5 billion by the year 2020. Rise in inhabitants, insufficient resources of medications in certain parts of the world, prohibitive cost of treatment for common ailments, side effects of several allopathic medicines in current usage and advancement of protection from at present utilized prescriptions for irresistible ailment have lead to increased prominence on the usages of plant resources as basis of medicines for the wide variety of human ailments. India due to its wide range of geographical, ecological and biological diversities possesses many species that are directly or indirectly cast-off as sources of herbal, allopathic or homeopathic medicines. A significant number of the non-industrial nations practice conventional medication as its primary wellspring of medical services, which is ordinarily of plant beginning [12,13]. Today, almost 88% of the worldwide populaces switch to plant based drug as their first line of safeguard for supporting wellbeing and fighting diseases [14, 15]. Considerable research on pharmacotherapy has been carried out on Indian medicinal plants, which are also rich sources of antioxidants.

Hepatocellular diseases

Today, human beings are exposed on a daily basis to certain foreign chemicals collectively referred to as xenobiotics which are causing serious health problems. Many of these are relatively insoluble in water, soluble in fats and they incline to screen into the hydrocarbon layer of membranes and the fat globules of adipose cells rather than being excreted in the urine. Thus they accumulate in the body

with deleterious consequences. Liver is an essential organ that assumes a significant part in digestion and discharge of toxicants from the body. Liver toxicity is a significant medical issue that challenges medical care experts as well as the drug business and medication administrative organizations. Hepatic injury caused by various drugs (anti-biotics, antituberculosis drugs, chemotherapeutic agents, carbon tetrachloride, thioacetamide etc.), extreme consumption of alcohol, microbes is well-documented. The liver disorders are worldwide health problem. It is a vital organ for drug metabolism and appears to be profound target site for substances modulating biotransformation. Despite frequent occurrence of liver ailments with great morbidity and mortality, its medical management is currently inadequate and no therapy has been developed which successfully prevent the progression of hepatic diseases. Although newly developed drugs are being used to treat chronic hepatic disorders but they often impose side effects [16,17].

Hepatic damage results in jaundice, fatty liver, cirrhosis, and hepatitis [18-20]. The common causative agents of liver injuries are toxic chemicals, antibiotics, antitubercular drugs, alcohol, hepatitis virus and malarial parasites. Acetaminophen and isoniazid are also inducing hepatotoxicity in human. Isoniazid and rifampicin, the first line drugs used for tuberculosis therapy are associated with hepatotoxicity [21]. Hepatic ailment rate has been accounted for to remain a lot higher in agricultural nations like India (8-30%) compared to that advanced countries (2-3%) [22]. Alcohol-related problems now rank among the world's major public health concerns, not only in most developed countries but also in emerging countries including India. The WHO assesses that there are around 2 billion individuals overall who burn-through cocktails and 76.3 million with diagnosable liquor use issues. Overall, there is a causal relationship between alcohol consumption and around 60 types of diseases and injury. Studies among student population in India have reported the use of alcohol to be 12.7 % in high schools, 32.6 % in universities and 9.3 to 15.1 % among college students. Significant no of deaths/diseases are found in different states of India due to alcoholism [23].

Hepatoprotective plants

Natural plants or plant based medications have been used for the most part by botanist, researcher, and analyst universal for the counteraction and treatment of liver disease. Significant examinations have been completed on ethnomedicinal plants; in any case, least complex few restorative plants have pulled in the interest of researchers, to look at them for a treatment of hepatic change (Table 1.) Clinical exploration in this century has affirmed the viability of a few floras in the management of liver alterations. Subsequently, this audit pays to the information on revealed native plants, which are pervasive for treatment of liver disorders.

Azadirachta indica (Meliaceae)

Hepatoprotective impact of *Azadirachta indica* leaves powder was considered in contrast to CCl₄ initiated liver diseases. The assessment markers utilized were SGOT, SGPT, ALP, glucose, bilirubin, cholesterol and protein. These biochemical indices were essentially changed because of dose of CCl₄, yet the aqueous leaves extract of *Azadirachta indica* fundamentally recuperates all markers to normal levels. Silymarin was utilized as a norm for correlation. This demonstrates generally speaking promising impact against liver issues [24].

Andrographis lineata nees (Acanthaceae)

Hepatoprotective effect of *Andrographis lineata* extracts in CCl₄ induced liver injury in rodents. Animal intoxicated with subcutaneous injection of 50% v/v CCl₄ in liquid paraffin. Biochemical constraints such as SGOT, SGPT, SALP and serum bilirubin were assessed to measure the proper functioning of liver. Histological observation of hepatic tissue supported the biochemical deviations. Extracts activity were also comparable to a standard drug [25].

Aegle marmelos (Rutaceae)

Aegle marmelos leaves which is likewise called as Bilva in antiquated Sanskrit, was utilized as natural medication in the Indian System of medication. The hepatoprotective impact of *Aegle marmelos* in alcohol-induced liver damage was evaluated in rats using vital LFTs biomarker. Singanan study on animal model represented that *Aegle marmelos* leaves have an excellent hepatoprotective efficacy [26].

Cassia roxburghii (Fabaceae/ Leguminosae)

Cassia roxburghii seeds has been used in ethnomedicine for various liver issues for its hepatoprotective activity. The methanolic concentrate of *Cassia roxburghii* turned around the toxicity delivered by carbon tetrachloride in portion subordinate way. The concentrate at the dosages of 250 mg/kg and 500 mg/kg are comparable to the effect produced by Liv-52 against hepatotoxins [27].

Cleome viscosa (Capparidaceae)

The hepatoprotective efficacy of the *Cleome viscosa* Linn extract was evaluated in carbon tetrachloride induced hepatotoxic rats. Plant extract found operational as protection of liver. The hepatoprotective activity of alcoholic extract was comparable to that of silymarin, a standard hepatoprotective drug [28].

Coccinia grandis (Cucurbitaceae)

Fruits extract of *Coccinia grandis* Linn evaluated against CCl₄ prompted hepatotoxicity in rats and levels of AST, ALT, ALP, total proteins, total and direct bilirubin were evaluated. At a dose level of 250 mg/kg, the alcoholic extract decreased the LFTs biomarkers which were comparable to that of silymarin revealing its hepatoprotective effect [29].

Cichorium intybus (Asteraceae)

It is used as anti-hepatotoxic, antiulcerogenic, anti-inflammatory, appetiser, cardiogenic, depurative, diuretic, and contains a variety of bioactive compounds, like, inulin, sesquiterpene lactones and coumarins, which plays a key role in medicinal and dietary purposes [30].

Ficus carica (Moraceae)

The methanolic extract of *Ficus carica* Linn. was evaluated for hepatoprotective activity in CCl₄ induced liver damaged rats. Oral dose of methanolic extract at 500 mg/kg showed a significant defending reflected by depressing the levels of AST, ALT, total serum bilirubin, and malondialdehyde equivalent, an index of lipid peroxidation of the liver [31].

Prosthechea michuacana (Orchidaceae)

Prosthechea michuacana also studied against carbon tetrachloride induced hepatic ailments in wistar rats. Methanolic extract treated group of animal reduced hepatotoxicity at dose-dependant manner. This hepatoprotective movement is comparable with silymarin. Other chemical extract like Hexane and chloroform has not shown any specious effect. The discoveries demonstrated that the methanolic concentrate of *Prosthechea michuacana* can be a likely premise of anticipated hepatoprotective methods [32].

Phyllanthus reticulatus (Euphorbiaceae)

Phyllanthus reticulatus extract was tested for the hepatoprotective efficacy in animal model alongside carbon tetrachloride induced liver impairment. The animal receiving the extract showed encouraging hepatoprotective efficacy as apparent from noteworthy changes of pentobarbital induced sleeping period, changes the LFTs biomarkers and liver histology of as compared to CCL₄ toxicated rats [33].

Rheum emodi (Polygonaceae)

Commonly known as Indian Himalayan Rhubarb, the major constituents are anthraquinones. It is cast-off as a laxative, diuretic to treat kidney stones, gout and jaundice. Its hepatoprotective effect is reported [34]. It contains chrysophanic acid, emodin, glucose rhapatein, tannin, gallic acid and lignan.

Solanum nigrum (Solanaceae)

The defensive impacts of aqueous concentrate of *Solanum nigrum* against liver toxicity were assessed in CCl₄ incited ongoing hepatotoxicity in rodents. The outcomes showed that the treatment of *Solanum nigrum* essentially brought down the CCl₄ incited serum levels of hepatic protein markers, superoxide and hydroxyl extremists. *Solanum nigrum* could secure liver against the CCl₄ actuated oxidative harm in rodents, and this hepatoprotective impact may be added to its regulation on detoxification catalysts and its cell reinforcement and free extreme forager impacts [35].

Morinda citrifolia (Rubiaceae)

The hepatoprotective effects of *Morinda citrifolia* juice was evaluated against CCl₄ tempted prolonged hepatic impairment in female Sprague Dawley rats. Serum alkaline ALP, AST, ALT, total cholesterol, triglycerides, LDL and VLDL levels were reduced with the *Morinda citrifolia* therapy. Thus, *Morinda citrifolia* juice appears to defend the hepatocytes from chronic exogenous CCl₄ exposures [36].

Morus alba (Moraceae)

Hepatoprotective effect of *Morus alba* also evaluated against N-Nitrosodiethylamine induced hepatotoxicity in rats. Animal intoxicated with subcutaneous injection of NDEA by dissolving it in milliQ water. Biochemical constraints such as SGOT, SGPT, SALP and serum bilirubin were assessed to measure the proper functioning of liver. LFTs Biomarker regains their normal level after the therapeutic dose of *Morus alba*. Histological observation of hepatic tissue supported the biochemical deviations. Ethanolic extracts of *morus alba* showed the highly effective results which were also comparable to a standard drug silimarin [37].

Leucas lavandulaefolia (Labiatae)

The aerial parts of *Leucas lavandulaefolia* Rees, was tested for hepatoprotective activity against CCl₄ in rats. Ethyl acetate extract of *Leucas lavandulaefolia* has shown significant activity, lowering the LFTs biomarkers in rats intoxicated with Carbon tetrachloride [38].

Vetiveria zizanioides (Poaceae)

Hepatoprotective efficacy of methanolic extract of *Vetiveria zizanioides* Linn root was studied against 20% ethanol tempted hepatic ailments in rats. Treatment with methanolic extractive of *V. zizanioides* and silymarin significantly prevented the functional, physical, histobiochemical changes induced by ethanol, representing the regaining of liver cells. These results demonstrate that methanolic extract of *V. zizanioides* root possessed the hepatoprotective activity [39].

Wedelia calendulacea (Asteraceae)

Ethanolic concentrate of *Wedelia calendulacea* L. has concentrated against CCl₄ instigated intense hepatotoxicity in rodents. The treatment with ethanolic concentrate of *Wedelia calendulacea* showed a portion subordinate decrease in CCl₄ initiated raised serum catalyst exercises with equal expansion in complete proteins and bilirubin, demonstrating the concentrate could improve the arrival of ordinary practical status of the liver [40].

Table 1. List of Hepatoprotective Plants

<u>S. No.</u>	<u>Plants</u>	<u>Liver Parameter</u>	<u>Citation</u>
1	<i>Acathopanax senticosus</i>	AST, ALP	[41]
2	<i>Ficus hispida</i>	GOT, GPT, bilirubin, ALP	[42]
3	<i>Rhazya stricta</i>	Pentobarbitone induced sleeping time, GSH, AST, ALT, gamma glutamyl transferase, cholesterol, liver weight	[43]
4	<i>Cassia fistula</i>	GOT, GPT, bilirubin, ALP	[44]
5	<i>Angelica sinensis</i>	ALT, hepatic nitric oxide synthase activities, GSH, MDA	[45]
6	<i>Silene aprica</i>	Morphological and biochemical observations.	[46]
7	<i>Trianthema portulacastrum</i>	GOT, GPT, ALP, bilirubin, total Protein	[47]
8	<i>Bauhinia racemosa</i>	GOT, GPT, ALP, SOD, CAT, LPO, GSH, bilirubin, total Protein	[48]
9	<i>Centaurium erythraea</i>	GPT, GOT, LDH	[49]
10	<i>Berberis tinctoria</i>	GOT, GPT, ALP, bilirubin, total protein, lipid peroxidation GSH, SOD, catalase activity	[50]
11	<i>Zingiber officinale</i>	ALT, AST, ALP, LDH, SDH	[51]
12	<i>Moringa oleifera</i>	ALP, AST, ALT, LPO and TBARS	[52]
13	<i>Ginkgo biloba</i>	ALT, AST, tumor necrosis factor alpha in blood, GSH, MDA.	[53]
14	<i>Aegle Marmelos</i>	TBARS, GSH, SOD, GPx, CAT,	[54]
15	<i>Calotropis procera</i>	GPT, GOT, ALP, bilirubin, cholesterol, HDL, tissue GSH.	[55]

16	<i>Raphanus sativus</i>	Thiobarbituric acid reactive substances, GOT, GPT, GSH, catalase.	[56]
17	<i>Phyllanthus polyphyllus</i>	AST, ALT, ALP, total bilirubin, LPO, total protein, SOD, catalase, GPx, GST	[57]
18	<i>Enicostemma littorale and blume and Eclipta alba</i>	AST, ALT, ALP, SOD, CAT, LPO and TBARS	[58]

Conclusion

Herbal and conventional botanical products had been used considering historical instances for the remedy of numerous issues and sicknesses. Those natural plants had been mentioned which have been formerly explored through numerous researchers for their hepatoprotective sports. Several medicinal plants show off now no longer simplest hepatoprotective activity, however additionally an extensive variety of anticancer, diuretic, antiarrhythmic, and diverse therapeutic approaches. Hepatoprotective plants are vital for the creation of medication which might be much less costly, have fewer facet consequences, are extra potent, and permit powerful remedy developed for hepatoprotection. Herbal cures are unfastened from facet consequences and toxicity, not like allopathic meds. Studies on hepatoprotective plants will make a contribution to the achievement of the populations needing herbal remedy for hepatotoxicity.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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